The Characteristics and Release of Diclofenac Sodium of Niosome System in Carbomer 940 Gel Base Preparation (Niosome System of Diclofenac Sodium-Span 20-Cholesterol with Molar Ratio 1:5 :5)

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Submission date: 09-Jan-2019 11:23AM (UTC+0800)
Submission ID: 1062403336
File name: Bukti_C-41_f.pdf (87.03K)
Word count: 2009
Character count: 10593

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Abstract

The present study was designed to determine characteristics and release of diclofenac sodium of niosome system in Carbomer 940 gel base preparation. The composition of niosome system is diclofenac sodium-Span 20-cholesterol with molar ratio 1:5:5. Niosome was prepared by reversed phase evaporation method. Formula I was Carbomer gel contain of niosome components that are not in niosome system. Formula II was Carbomer gel with the noisome system. The evaluation of noisome characteristics included morphologic test by light microscope and Scanning Electron Microscopy (SEM), and drug entrapment efficiency (Ep). The characteristics of the gel preparation (organoleptic and pH) were investigated and in vitro releases of diclofenac sodium through cellophane membrane into buffer phosphate saline (PBS) pH 7.4±0.05 at 37°C were studied. Flux and pH were analyzed by statistic programmed of SPSS 16.0 using Independent-sample t test with degree of believe 95% (α = 0,05). The result showed that the average of entrapment efficiency was 50.34 % ± 2.82. The characteristics of niosome system (formula II) preparation didn't have effect on consistency and color of diclofenac sodium gel preparation, but this system results specific odor if it was compared with that of control. The result showed that pH of formula I (control) was 6.23 ± 0.05 and formula II (niosome system) was 6.16 ± 0.11. Flux of diclofenac sodium in formula I was 55.03 ± 2.66 g/cm²/menit$^{1/2}$ and formula II was 55.07 ± 1.31 g/cm²/menit$^{1/2}$. The statistic analyze of pH and flux of diclofenac sodium showed that were not significant different between formula I and II.

Key words: diclofenac sodium, niosome, Span 20, Cholesterol, flux

Introduction

Diclofenac sodium is NSAID, the drug causes gastric irritation and undergoes hepatic first-pass metabolism (40-50%) (Ganiswara,1995). Diclofenac sodium has log P 1.13 (Budavari et al, 2001), so it hydrophobic compound and has small solubility in water and distribution in the gel based not well. One of the methods used to increase distribution in the gel based by made vesicle, niosome (Choi and Maibach, 2005). Niosome is well documented for transdermal drug delivery. Niosome system is unilamellar or multilamellar vesicle where in an aqueous solution is enclosed in highly ordered bilayer made up of nonionic surfactant with or without cholesterol and dicetyl phosphate (Biju et al, 2006). The factor that influence on characteristics include size of niosome vesicle, entrapment efficiency (Ep) and released was concentration and type of surfactant (HLB) also it contain of cholesterol (Patel, 2005). The research of Shahiwala and Misra (2002), niosome was made from active compound of Nimesulid and used Span 20-cholesterol with molar ratio 1:3:3 has given Ep 39.00±0.001%, and using molar ratio 1:6:6 the value of Ep was 91.21±0.010 %.

In this study, the influence of niosome system was made from diclofenac sodium, Span 20 and cholesterol with molar ratio 1:5:5 on preparation characteristics and released of diclofenac sodium from Carbomer 940 gel base was evaluated.

Methodology

Materials

Diclofenac sodium was obtained from PT Dexa Medika, Carbomer 940 (Noveon Asia Pacific Ltd, Hongkong), Span 20 (Sigma), Cholesterol (Sigma), KCl (E.Merck), NaCl p.a (E.Merck), $Na_2HPO_4.12\ H_2O$ p.a (E.Merck), KH_2PO_4 p.a. (E.Merck). trietanolamin was purchased from PT. Tristar. Compound was used without mention the specification was a pharmaceutical grade.

Preparation and characterization of niosome

The composition of niosome system showed in Table 1 and the formulation of sodium diclofenac gel preparations showed in Table 2.

Table1.The composition of niosome system.

Compound	Molar Ratio	Amount in 20 g preparation
Diklofenac Sodium	1	0.2000 g
Span 20	5	1.0904 g
Cholesterol	5	1.2204 g
Chloroform	-	10 mL
Aqua free of CO_2	-	9 mL
PBS pH 7.4	-	6 mL

Niosomes were prepared by using Reverse Phase Evaporation Technique (REV). The molar ratio of diclofenac sodium, Span 20 and cholesterol is 1:5:5. Drug, non ionic surfactant and Cholesterol were weighed as indicated in Table 1. Cholesterol and Span were dissolved in chloroform, diclofenac sodium in 9.0 mL aquadest than mixed and sonification at temperature 4-5^{0}C for 16 minutes. The mixture was added 6 mL PBS pH 7.4±0.05 and sonification again 12 minutes. Than the mixture was rotavapored at 40^{0}C, 200 mmHg until chloroform disappeared (± 1.5 h) and the end evaporated using waterbath at 60° C until 15 minutes to make the concentrated suspension of niosome system. Than the niosome system was adding into the Carbomer gel with the composition as indicated in Table 2.

Table 2. The formulation of diclofenac sodium preparation.

Compound	Formula	
	F I (Control)	F II (Niosome System)
Diclofenac Sodium	0.2000 g	-
Span 20	1.0904 g	-
Cholesterol	1.2204 g	-
PBS pH 7.4	6 mL	-
Chloroform	10 mL	-
Aqua free of CO_2	9 mL	-
Total amount of control	11.9978 g*	-
Niosome	-	12,0525 g**
Carbomer 940 (0.5%)	0.1000 g	0.1000 g
TEA	0.2 mL	0.2 mL
Aqua free of CO_2	Ad 20.0 g	Ad 20.0 g

* Total amount of the control after concentrated
** Total amount of niosome system

Determination of the entrapment efficiency of diclofenac sodium in the niosome system.

The entrapment of diclofenac in the niosome system was calculated using equation 1:

$$Ep\ (\%) = \left[\frac{(Ct - Cf)}{Ct}\right] x\ 100\% \text{.....(1)}$$

where,
Ep : diclofenac sodium entrapment in the niosome system
Cf : concentration of diclofenac free (un entrapped)
Ct : total concentration of diclofenac sodium in the formulation of niosome system.

Determination of pH on the formulation

The pH of preparation was done by mixed the preparation in the aqua free of CO_2 in ratio 1:9. Mix well and than the pH of preparation was measured using pHmeter.

Determination of diclofenac released from the preparation.

Permeation study was performed apparatus 5 paddle over disk completely with diffusion cell (Figure 1) at 37°C for 6 h. As a membrane was cellophane and as donor compartment was filled by preparation of niosome system in Carbomer 940 gel. As receptor solution was phosphate buffer saline pH 7.4. At the appropriate time sample was taken from receptor solution.

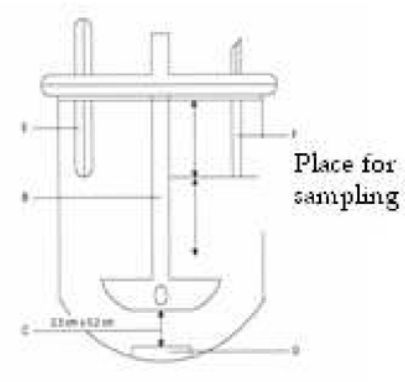

Figure 1. Apparatus 5-paddle Over Disk (The USP Convention, 2002)

Diclofenac concentration of sample solution was measured using Spectrophotometer. Released of diclofenac sodium was calculated using equation 2 (Higuchi, 1959).

$$Q = \frac{q}{x} = [\ Dt\ (2A - Cs)\ Cs\ ]^{1/2} \text{.....(2)}$$

where,
Q : flux of drug released
D : coefficient diffusion of drug in the based
A : concentration of drug in the based
Cs : solubility of drug in the based
t : time

Results and Discussions

The morphology of niosome system showed at the figure 2 and 3.

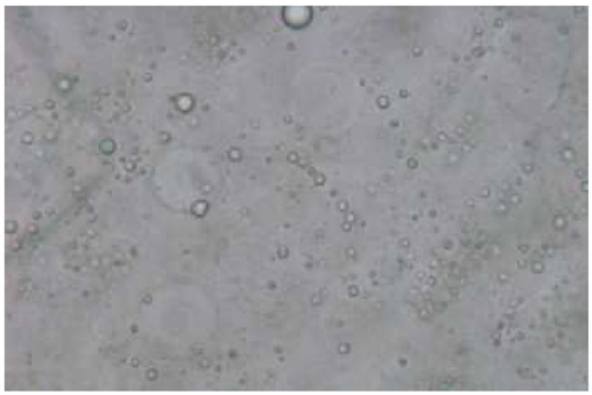

Figure 2. Morphology of noisome system using light microscope (Olympus BX 41) with magnify 1000X.

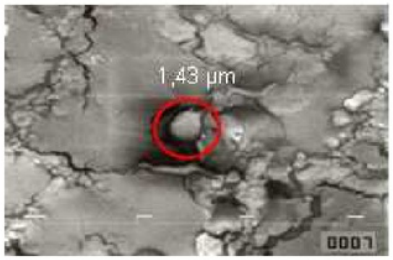

Figure 3. Morphology of niosome system using Scanning Electron Microscope (Jeol tipe JSM T-100)with magnify 3500X.

The percent entrapment of diclofenac sodium in the niosome system was shown at the Table 3.

Table 3. The entrapment efficient (Ep) of diclofenac sodium in niosome system

Replication	% Ep	Mean ± SD (%)
I	54,32	
II	48,19	50,34 ± 2,82
III	48,51	

The organoleptic of Carbomer gel of diclofenac preparation showed in Table 4.

Table 4.. The organoleptic of Carbomer 940 gel preparations of diclofenac sodium.
The pH value of diclofenac in Carbomer 940 preparations were shown at Figure 4.
Based on the statistical result of the pH using independent T-test that found there was insignificant different between control and niosom system preparation.

Formula	Observation		
	Consistency	Color	Smell
Control	Smooth and Viscous	White-Yellowish	No smell
Niosome System	Smooth and Viscous	White-Yellowish	Specific

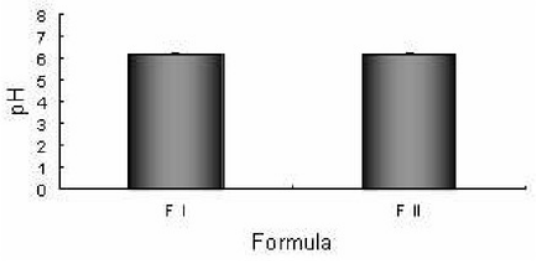

Figure 4. The pH value of diclofenac in Carbomer 940 preparations. Data were the mean of three replications ± SD.

Flux is the most useful index to evaluate the released of drug. The cumulative amount of drug released was plotted as function of root time. From the result of linear regression of steady state condition I get flux at the slope.

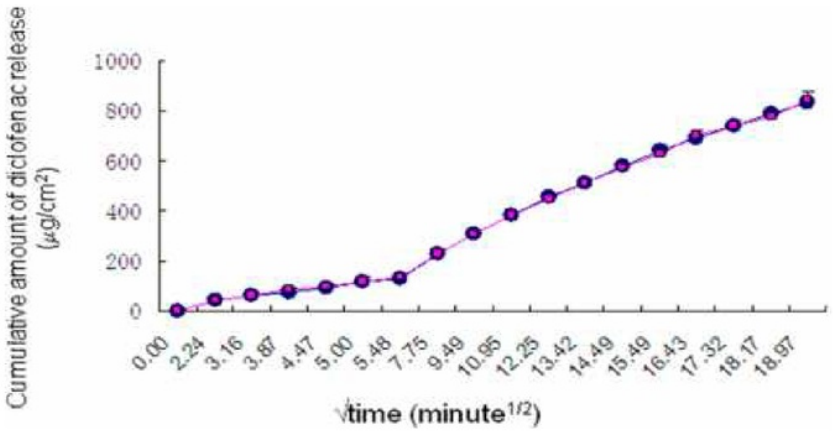

Figure 5. The profile of diclofenac released from the Carbomer 940 gel preparations. Data was the mean of three replications ± SD.(♦: Control; • Niosome System)

As shown in the Figure 5, the released profile shows the sufficient linearity with the coefficient r was ≥ 0.98.

Flux released of diclofenac sodium from Carbomer 940 gel base shown in Figure 6. In this Figure shown that the flux released of diclofenac from preparation of niosom system diclofenac sodium: Span 20: cholesterol with molar ratio 1:5:5 in Carbomer 940 gel base was insignificantly different compared with that of control. It caused the niosome system that used in the formulation was without separated the entrapment and not entrapment. So the profile was similar. Beside that maybe it caused the experiment was done only until 6 hours.

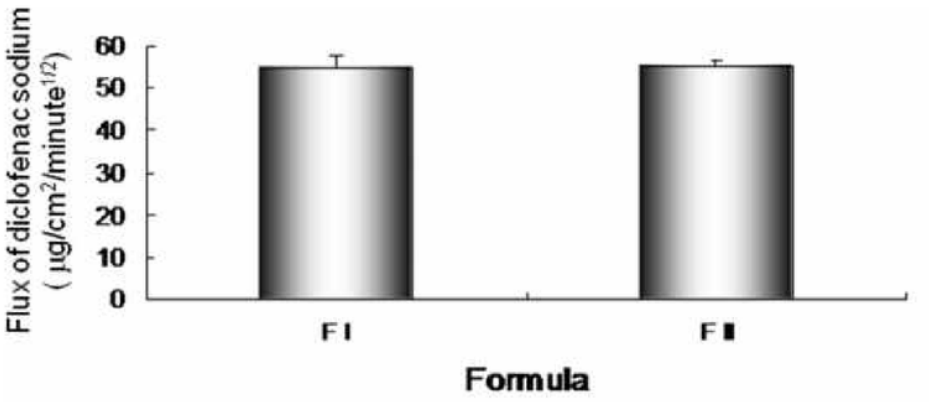

Figure 6. Flux released of diclofenac from Carbomer 940 gel base. Data was the mean of three replications ± SD.

From the results of the experiment we suggest that the experiment must done longer than 6 hours and the vesicle of niosome is separated from diclofenac sodium that is not entrapment in the vesicle.

Conclusion

The drug entrapment efficiency (Ep) of the niosome system of diclofenac sodium:Span 20:cholesterol (1:5:5) was 50,34 ± 2,82%.

The characteristics of niosome system preparation (formula II) didn't have effect on consistency and color of diclofenac sodium gel preparation, but this system results specific odor if it was compared with that of control. The pH of formula I (control) was 6.23 ± 0.05 and formula II (niosome system) was 6.16 ± 0.11, but there was not a significant difference between each formula.

The flux of diclofenac sodium release in control formula was 55.03 ± 2.66 μg/cm²/minute½ and formula of the niosome system was 55.07 ±1.31 μg/cm²/minute½. The statistic result of the flux of diclofenac released showed that there was not a significant different.

References

Biju, S.S., Talegaonkar S., Mishra P.R. And Khar R.K., 2006. Vesicular Systems: An Overview. Indian J. Pharm Sci, 68 (2): 141-153

Budavari, S., 1996. The Merck Index 12th. USA: Merck & CO., INC. p. 521

Choi, M. J., Maibach, H. I., 2005. Liposomes and Niosomes as Topical Drug Delivery Systems, Skin Pharmacology and Physiology 2005, J. of Pharmacol. and Biophis. Res., Vol. 18, No.5, p.209-219.

Ganiswarna, S. G., 1995. Farmakologi dan Terapi, Edisi IV, Jakarta: Bagian Farmakologi FKUI, hal. 207-210, 218.

Higuchi, T., 1959, Physical Chenical Analysis of Percutaneous Absorption Process From Creams and Ointments. Presented September 23-24, 1959, Seminar, New York City.

Patel, R. P., 2005. Niosome : An Unique Drug Delivery System, http://pharmainfo.net. Tanggal akses 11 November 2008

Shahiwala, A., Misra, A., 2002. Studies in Topical Application of Niosomally Entrapped Nimesulide, J. of Pharm. Sci, Vol. 5, No. 3, p 220-225.

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